Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 2, 4-7, 10-21, 23 and 26-36 are pending in the application, with claims 2, 17 and 19 being the independent claims. Claims 1, 3, 8, 9, 22, 24 and 25 were cancelled previously. Claim 19 was withdrawn previously.

Claims 2, 17 and 23 are amended herewith. Support for the amendments to the claims can be found throughout the specification, e.g., paragraphs [0010], [0012], [0015], [0028], [0030], [0036] and [0052] of the published application. New claims 26-36 are sought to be entered. Support for the new claims can be found throughout the specification, e.g., paragraphs [0029] and [0030] of the published application. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 2, 4-7, 10-18, 20, 21 and 23 were rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Rubin (U.S. Pat. No. 5,034,415) in view of Katz et al. (U.S. Pat. No. 5,925,669) in further view of Remmereit et al. (U.S. Pat. No. 6,440,931) and Harris (Diabetes Care 20:1859-1862 (1997)). Applicants respectfully traverse this rejection.

To establish a prima facie case of obviousness, the Supreme Court, in *KSR International v. Teleflex, Inc.*, 550 U.S. 398 (2007), clarified the requirements for

obviousness analysis under 35 U.S.C. § 103(a). *KSR* reiterated the importance of the Graham factors, including considering: (1) the scope and content of the prior art; (2) differences between the prior art and the patent claims; and (3) the level of ordinary skill in the art, and further noted that secondary considerations such as unexpected results are objective evidence of non-obviousness. *Id.*, citing Graham v. John Deere, 38 U.S. 1, 17-18 (1966). The Court in *KSR* also noted that the analysis supporting a rejection under 35 U.S.C. § 103(a) should be made explicit, and that it was "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed. Id. "To the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these 'identified, predictable solutions' may present a difficult hurdle because potential solutions are less likely to be genuinely predictable." *Eisai Co. v. Dr. Reddy's Labs, Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008).

The Office Action alleged that Rubin "teaches that the EPA and/or DHA **need not** be administered as **the free fatty acids per se**." Office Action at 2, citing Rubin, col. 5, lines 32-35. The Examiner then used this citation to concluded that "Rubin teaches the composition comprising DHA and/or EPA ***in general*** is useful for the treatment of diabetes mellitus." Office Action at 2 (emphasis added).

Applicants respectfully disagree with the Examiner's characterization of the art. The **full** citation that the Examiner referred to recites:

> [t]he EPA and/or DHA need not be administered as the free fatty acids per se, but may be used **in the form of their pharmaceutically acceptable salts**, or any other **pharmaceutically acceptable solid salt**, as these are suitable for making into orally ingestible tablets.

Rubin at col. 5, lines 32-37 (emphasis added). Thus, Rubin teaches that EPA and/or DHA can be administered either as a free fatty acid **or** in the form of a pharmaceutically

acceptable salt of a fatty acid. No mention of other forms of DHA or EPA are contemplated or described by Rubin for use in the treatment of a diabetic individual. In fact, the use of "free fatty acids" is reiterated throughout Rubin's specification and claims. Thus, based on the disclosure of Rubin, one of skill in the art would NOT have looked to the triglyceride or ester forms of these fatty acids to treat a diabetic individual.

Furthermore, the prior art as a whole fails to provide a reasonable expectation of success in practicing the claimed method. Prior art fails to provide the requisite reasonable expectation of success where it teaches one merely to pursue a general approach that seems to be a promising field of experimentation, where the prior art gives only general guidance as to the particular form of the claimed invention or how to achieve it.

The unpredictable nature of the art is referred to in the application as filed. For example, paragraph 8 of the published application states, "[s]tudies on the effect of polyunsaturated fatty acids on glucose control in diabetic and pediatric patients have to this point been inconclusive." The published application goes on to describe studies succeeding Rubin wherein fish oil administration was seen to effect triglyceride levels, but lack effect on glycemic control (Friedberg, C.E., *Diabetes Care* 21:494-500 (1998) and Montori et al., *Diabetes Care* 23: 1407-1410 (2000)). Since the prior art was inconclusive as to the effect of polyunsaturated fatty acids on diabetic patients, a person of skill in the art would have had no reasonable expectation of success that oral administration of the claimed dosage form would have the intended effect.

Furthermore, Applicants note that the present invention is directed to a method comprising administration of at least 1000 mg per day of DHA in the form of a triglyceride oil or ester that is substantially free of EPA. As depicted in Figure 1,

Applicants found that patients treated with 1000 mg/day of DHA containing oil for 12 months were found to have significantly lower HbA1c levels compared to patients treated with 200 mg of DHA per day for 12 months. A person of skill in the art would not have had any expectation of this result due to the unpredictable nature of the art as a whole.

Neither Katz, Remmereit, Harris, nor any combination thereof cure the deficiencies of Rubin. Katz is relied upon by the Examiner as allegedly providing a source of DHA substantially free of EPA. However, Katz does not provide any nexus or reason why one would use DHA (1) in the form of a triglyceride oil or an ester, (2) in an amount of at least about 1000 mg per day, and (3) substantially free of EPA for reducing HbAc1 levels. Certainly Katz does not provide a reasonable expectation of success in practicing the claimed method. Remmereit is relied upon by the Examiner as allegedly teaching HbA1c as a useful index of hyperglycemic stress, and as allegedly teaching the use of various anti-hyperglycemic agents. However, Remmereit does not provide any nexus or reason why one would use DHA (1) in the form of a triglyceride oil or an ester, (2) in an amount of at least about 1000 mg per day, and (3) substantially free of EPA for reducing HbAc1 levels. Certainly Remmereit does not provide a reasonable expectation of success in practicing the claimed method. Harris is relied upon by the Examiner as allegedly teaching comparison of diagnostics categories in the U.S. Population. Certainly Harris does not provide a reasonable expectation of success in practicing the claimed method.

Accordingly, none of the cited references alone or in any combination teach the method of the present invention for reducing HbAlc levels in a diabetic patient in need thereof. Likewise, even a combination of the cited references fails to provide any

reasonable expectation of success. Thus, a *prima facie* case of obviousness has not been established. For at least the above reasons, Applicants respectfully submit that the rejection of claims 2, 4-7, 10-18, 20, 21 and 23 under 35 U.S.C. § 103 be withdrawn.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: June 1, 2010

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